Remarks/Arguments:

A paper, i.e., "Amendment," is concurrently filed via hand carry to the PTO mailroom, in order to submit amendments to the drawings, which cannot be filed by facsimile. By the "Amendment" replacement sheets are submitted for application figures 14 and 15, in response to the drawings' objection. As required in the Office Action, each replacement sheet representing figures 14 and 15 (submitted with the Amendment) is individually identified by the figure number followed by a letter, i.e., the replacements sheets are identified as figures 14A-14C and 15A-15F.

The specification is amended, hereby, to be commensurate with the amendments to the drawings effected, hereby, i.e., figure 14 is, now, identified in the specification as Figures 14A-14C and figure 15 is now identified as figures 15A-15F.

The specification is amended, hereby, to insert the sequence identifier in the Sequence Listing that corresponds to each of the sequences found on page 14, i.e., SEQ ID NO: 9 and SEQ ID NO: 10, as required in the Office Action. The specification is further amended, hereby, to recite "SEQ ID NO:" in place of "SEQ ID NO." (each occurrence), as required in the Office Action.

Claims 39-54 are pending.

Claims 42, 52, 53, and 54 are amended, hereby, to address rejections of the claims as explained, below.

Claims 55-76 are cancelled, hereby, without prejudice or disclaimer, pursuant to withdrawal of the claims as being subject to restriction under 35 USC 121. Specifically, Applicants reserve the right to prosecute the subject matter of the cancelled claims in one or more divisional applications.

Claims 52, 53 and 54 were rejected under 35 USC 101 for allegedly defining non-statutory subject matter, i.e., subject matter that could not be distinguished from that found in nature. Reconsideration is requested in view of the instant amendment, whereby, the rejected claims are amended to recite "An isolated protein molecule."

The term "isolated" as used herein is considered to refer to molecules that are removed from their natural environment, i.e., isolated from a cell or from a living organism in which they normally occur, and that are separated or essentially purified from the coexisting components with which they are found to be associated in nature. This notion further means that the sequences encoding such molecules can be linked (by the skilled person in the art) to polynucleotides, to which they are not linked in their natural state, and that such molecules can be produced by recombinant and/or synthetic means as, for example, described on page 33 of the instant application. Even if for said purposes those sequences may be introduced into living or non-living organisms by methods known to those skilled in the art, and even if those sequences are still present in said organisms, they are still considered to be isolated.

Claims 39-54 are rejected under 35 USC 101 for allegedly lacking credible utility. Reconsideration of the rejection is requested, as follows.

According to the statement of rejection, the instant application does not disclose a specific biological role for the protein described and claimed or its significance to a particular disease. Therefore, it is alleged that the protein described and claimed should be an "orphan protein" in the art. Applicants submit that there might be a misunderstanding of the subject-matter presently

claimed, as the DNA of the instant application has not been isolated because of its similarity to a known DNA.

The DNA of the instant application has not been isolated because of its similarity to a known DNA. Rather, the nucleic acid molecule was discovered by a differential display experiment comparing different brain tissue samples with each other, whereby, said samples were derived, inter alia, from patients suffering from Alzheimer's disease (page 31 and figures 2 and 16 of the subject application). The detection of this molecule was only possible because it plays a specific biological role in the context of a particular disease and thus has a profound significance to a particular disease, namely, Alzheimer's disease.

After discovering and isolating this nucleic acid molecule, it was examined and its specific biological role characterized. Its biological role and its utility as a diagnostic marker, for instance, specifically rely on its detection in connection with Alzheimer's disease. Thus, the presently claimed protein (subject matter) of the instant invention is no an "orphan protein," as termed in the statement of rejection; it was discovered due to its specific function and due to its effect in the process of a particular neurodegenerative disease, i.e., Alzheimer's disease. If samples of healthy persons or of persons suffering from another disease are examined, said protein would not have been recognized, even if it were similar to a known DNA or protein.

According to the statement of rejection there are many proteins are differentially expressed in the areas of neuronal degeneration within Alzheimer's disease brain compared to healthy control brains. Careful review of the prior art dealing with studies of gene-expression changes associated

with Alzheimer's disease pathology shows that the person skilled in the art would have considered that an estimated average of approximately 2% of all protein-encoding human gene transcripts studied, so far, have shown changes in expression and, further, that these changes in gene expression can, indeed, be involved in the progression of dementia.

It is by no means trivial to identify differently expressed genes from the large pool of genes expressed in any given tissue and for any given disease. Further, it is not trivial to establish and correlate a function of such a differentially expressed gene in the progression of a disease.

As acknowledged in the statement of rejection applicants have described and claimed (in the subject application) that the protein SELADIN-1 has specific properties and specific biological characteristics, which are of high value for the utility of said protein. For instance, the benefit that results from the property to protect cells against degeneration and cell death is fully described by disclosing viability assays (pages 27 and 28 and figure 20 of the subject application). Further, the use of SELADIN-1 as a diagnostic marker in a number of applications, and the ability of making a diagnosis for a particular neurodegenerative disease, which is a very valuable and practical "real world" utility, is provided (for instance, on pages 5-8 and 11and in figures 4 and 17 of the subject application). Additionally, the practical use of vectors harboring DNA encoding the protein SELADIN-1 is disclosed (for example, on pages 31 and 33 and in figures 18, 20, and 21 of the subject application). Thus the presently claimed invention has a practical utility, which utility is disclosed in the subject application. As such, the utility requirements of §101 are met for the

presently claimed invention and, so, withdrawal of the rejection of claims 40, 45, and 53 under §101 is in order.

Claims 1, 2, and 4 are rejected under 35 USC 112, ¶1, for allegedly lacking enabling disclosure on how to use the claimed invention. As the rejected claims were previously cancelled, the rejection is in order for withdrawal.

Claims 40, 45, and 53, were rejected under 35 USC 112, ¶1, for allegedly lacking a written description of the invention, i.e., a description allegedly failing to show that applicants had "possession of the claimed invention." Reconsideration of the rejection is requested, as follows.

The statement of rejection acknowledges that the instant specification satisfies the written description requirements of §112, ¶1, i.e., applicants had "possession" of the subject matter in the rejected claims for the nucleic acid molecule having the sequence SEQ ID NO: 2 (in the Sequence Listing) - the nucleic acid encoding the protein of SEQ ID NO: 1.

The statement of rejection alleges that the instant application fails to satisfy the written description requirements of §112, ¶1, i.e., that applicants allegedly did not have "possession" of the "functional variant" subject matter in the rejected claims. The statement of rejection relies on there allegedly being no "species or genus" exemplified in the specification for the claimed *genus* "functional variant" (Office Action page 10) and, further, on an alleged "lack of guidance or teaching regarding structure . . . [as related to] function," thereof (Office Action page 9). The rejection cannot be maintained because it is based on reasoning that fails to apply the correct standards for

determining whether the written description requirement of §112, ¶1, is satisfied with respect to a claimed *genus*.

"Mention of representative compounds encompassed by generic claim language clearly is not required by §112 or any other provision of the statute." *In re Robins*, 166 USPQ 552, 555 (CCPA 1970)."[I]t is not necessary to . . . describe in the specification all possible forms in which the claimed principle may be reduced to practice." *Smith v. Snow*, 294 U.S. 1, 11 (1935). Under §112, first paragraph, the concern of the USPTO is support or non-support for a generic term, not its breadth. *In re Marcozzi*, 169 USPQ 367, 369 (CCPA 1971). The first paragraph of §112 contains no requirement for a *structural* disclosure - a description entirely in *functional* terms satisfies the requirement. *Ex parte Butler*, 217 USPQ 290 (USPTO Bd. App. 1982). *See*, also, *In re Donohue*, 193 USPQ 136 (CCPA 1977), and *Ex parte Billottet*, 192 USPQ 414 (USPTO Bd. App. 1976).

As indicated, above, the rejection relies on the allegation that the specification does not exemplify any "functional variant" of SEQ ID NO: 1, as presently claimed. Since "[m]ention of representative compounds encompassed by generic claim language clearly is not required by §112 or any other provision of the statute," *Robins*, 166 USPQ at 555, the reliance is misplaced.

As also indicated, above, the rejection relies on their allegedly being insufficient disclosure relating "structure and function" of the claimed "functional variant." Since a written description entirely in *functional* terms satisfies the requirements of §112, ¶1, *Butler, supra*, the reliance is misplaced.

Accordingly, as the rejection of claims 40, 45, and 53 relies on incorrect standards for determining whether the written description requirement of §112, ¶1, is satisfied with respect to the presently claimed *genus* "functional variant," the rejection cannot be maintained and, so, is in order for withdrawal.

Moreover, the Examiner's definition of a claim limitation cannot conflict with the definition given in the specification. *In re Zletz,* 13 USPQ2d 1320, 1322 (Fed. Cir. 1989). In this respect, attention is directed to the precisely defined meaning of "functional variant" set forth in the instant specification (pages 2-3). As specified, "variants" of a protein molecule shown in SEQ ID NO: 1 include, for example, polypeptides with conservative amino acid substitutions in highly conservative regions, which refers to any polypeptide, in reference to the polypeptide molecule disclosed in the present invention in which one or more amino acids are substituted at the N-terminus, and/or the C-terminus, and/or within the narrative amino acid sequence of the native polypeptide of the present invention. "Functional variants" include variants of SEQ ID NO: 1 which, despite modifications of a given primary structure, exhibit an essentially unaffected biological function similar or identical to the function of a polypeptide of SEQ ID NO: 1, i.e., as described in the instant invention, to protect cells from degeneration and/or cell death. Thus, the appropriately narrow and clear specification of the term "variant", i.e. functional "variant", leaves no doubts about the scope of said functional variant of the sequence of SEQ ID NO: 1. A person skilled in the art will be able to check the function of such "variants," namely, the function of protecting cells from degeneration and/or cell death.

Claims 42, 43, 44, and 49 were rejected under 35 USC 112, ¶2, for allegedly being indefinite. Reconsideration of the rejection is requested in view of the amendments to the claims effected, hereby, and the remarks as follows.

The expression "in particular" is deleted, hereby, from claim 42, as suggested by the Examiner. As such, claim 42 reads: "An isolated nucleic acid molecule of claim 41, wherein the nucleic acid molecule is a cDNA molecule comprising a nucleotide sequence shown in SEQ ID NO: 2."

As for claim 43 being allegedly indefinite for reciting "under stringent conditions" with respect to hybridization conditions, attention is directed to page 3 of the instant specification, where an example of stringent hybridization conditions is provided. Thus, the applicants submit that claim 43 is not indefinite.

The statement of rejection alleges that there is no basis in claim 46 for the limitation "a plasmid" in claim 49. Claim 49 is not dependent on claim 46. Claim 49 is dependent on claim 47, which provides antecedent basis for "the plasmid."

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Favorable action is requested.

Respectfully submitted,

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